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BRIEF REPORT

Misidentification of *Yersinia pestis* by Automated Systems, Resulting in Delayed Diagnoses of Human Plague Infections—Oregon and New Mexico, 2010–2011

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One human plague case was reported in Oregon in September 2010 and another in New Mexico in May 2011. Misidentification of *Yersinia pestis* by automated identification systems contributed to delayed diagnoses for both cases.

Plague is a flea-transmitted bacterial infection caused by *Yersinia pestis*. Primarily a disease of rodents, it is enzootic in the western United States. Humans are infected through bites from infected rodent fleas, direct contact with tissues from an infected animal, or, rarely, through respiratory droplets. The majority of human cases occur during epizootic periods when rodents die and infected fleas search for new hosts [1, 2]. The incubation period is 1–7 days [3]. The most common clinical presentation of plague is the bubonic form, characterized by fever and swollen, painful regional lymph nodes or buboes. Early diagnosis and treatment with gentamicin, streptomycin, doxycycline, or chloramphenicol are critical to reducing mortality and preventing secondary manifestations such as septicemia or pneumonia [4]. Delayed recognition may lead to nosocomial exposures among healthcare workers who drain buboes or provide care to pneumonic plague patients and do not follow droplet precautions or among laboratorians who unknowingly handle *Y. pestis* isolates and do not follow proper biosafety level 2 precautions.

From 1990 to 2010, 142 confirmed human plague cases were reported in the United States, predominantly in Arizona, California, Colorado, and New Mexico. Of the 139 cases for which there were clinical data, 104 (75%) were bubonic plague (7% mortality), 29 (21%) were septicemic plague (24% mortality), and 6 (4%) were pneumonic plague (50% mortality) (Centers for Disease Control and Prevention, unpublished data, 2011).

Because of the potential for person-to-person transmission and because it threatens public health, *Y. pestis* is considered a potential bioterrorism agent. Clinical microbiology laboratory guidelines have been developed in the United States to aid in its quick identification [5, 6]. However, identification of *Y. pestis* still can be challenging given the rarity of the disease; lack of clinical suspicion, even in enzootic areas; and increasing dependence on automated systems for bacterial identification in clinical laboratories. Automated systems are used in the majority of clinical microbiology laboratories and are heavily relied on to promptly identify organisms. We report 2 human plague cases that were misdiagnosed clinically and misidentified by multiple automated systems.

CASE 1

On 27 August 2010, a 17-year-old female from Oregon was admitted to the hospital with abdominal pain, painful bilateral inguinal lymphadenopathy, and hypotension. During the week prior, she had experienced a temperature of 39.4°C with chills and weakness. She visited her primary care physician and received empiric treatment with azithromycin.

Clinical examination at the hospital revealed bilateral swollen inguinal lymph nodes, a palpable spleen, and an enlarged liver. Blood cultures were collected. Laboratory tests revealed elevated transaminases (4 times the upper limit of normal), thrombocytopenia, and acute renal failure. Computed tomography (CT) of the abdomen indicated a limited number of periaortic lymph nodes <1.5 cm and pelvic inflammation. She received piperacillin-tazobactam and clindamycin therapy and was transferred to another hospital the next day for renal monitoring. Leptospirosis was suspected, and clindamycin was changed to doxycycline. Later that day, the initial blood culture grew a gram-negative rod with bipolar staining.

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She started to improve on 29 August and was discharged home on 2 September with a 2-week regimen of oral amoxicillin and doxycycline. She recovered fully.

The gram-negative isolate was sent to 3 commercial laboratories for identification. On 2 September, it was identified at the first hospital's commercial reference laboratory as *Acinetobacter lwoffii* by using a Microscan Instruments automated system (Siemens, New York City). On 4 September, the commercial laboratory located in the second hospital to which the patient had been transferred identified the isolate as *Pseudomonas luteola* by using a Vitek2 automated system (bioMérieux, Inc., Durham, NC) (probability 90%). Because of discrepant results and by physician request, repeat testing was performed at that laboratory by using a BBL Crystal miniaturized rapid identification system (Becton, Dickinson, and Company, Franklin Lakes, NJ), which identified the isolate as *Yersinia pseudotuberculosis* on 16 September. The isolate was then sent to a third laboratory at which a Phoenix automated system (Becton, Dickinson, and Company) identified it as *Y. pseudotuberculosis* on 19 September (confidence value 96%) and an API 20 E strip (bioMérieux) identified it as *Y. pestis* on 20 September. This laboratory forwarded the suspect *Y. pestis* isolate to the regional public health laboratory. Finally, on 21 September, *Y. pestis* was identified by direct fluorescent antibody (DFA) testing and confirmed by polymerase chain reaction and bacteriophage lysis at the public health reference laboratory in Spokane, Washington, and reported to the public health authorities.

CASE 2

On 23 April 2011, a 58-year-old male with chronic renal insufficiency presented to an emergency department in New Mexico with a temperature of 38.9°C and left-lower abdominal and inguinal pain after a 9-mile walk the previous day. A blood culture was collected, and the patient was discharged home with acetaminophen. He was admitted to the hospital the following day for persistent fever and abdominal pain. Laboratory tests revealed thrombocytopenia and acute worsening of renal function. On 25 April, another set of blood cultures was collected. A CT of the abdomen displayed diverticulosis and nonspecific inflammatory fluid in the left inguinal area. The patient received piperacillin-tazobactam for diverticulitis. Blood cultures obtained on 23 April and 25 April grew a gram-negative rod on 24 April and 26 April, respectively. On 26 April, the patient was transferred to another hospital for further evaluation, and therapy was changed to a 10-day regimen of ciprofloxacin and metronidazole.

The gram-negative isolate from the 25 April blood culture was forwarded to a commercial laboratory, where it was identified on 2 May as *P. luteola* (probability 96%) by using a Vitek2. On 1 May, the same commercial laboratory tested an isolate from the 23 April blood culture and identified the organism as *Y. pestis* (probability 87%); however, this was not officially reported. Due to the low probability, the isolate was tested again on 2 May and identified as *Y. pseudotuberculosis* (probability 94%) using the same system. The clinical microbiologist at the first hospital was suspicious of these discrepant results and called the New Mexico Department of Health Scientific Laboratory Division (SLD). The isolate from 23 April was sent from the original clinical laboratory to SLD where *Y. pestis* was identified by DFA testing on 5 May and confirmed by bacteriophage lysis on 6 May. The patient was discharged from the hospital on 6 May and recovered fully.

DISCUSSION

In both the Oregon and New Mexico cases, plague was not suspected clinically and *Y. pestis* was not confirmed until weeks after initial presentation. These cases illustrate the challenge for clinicians in suspecting this rare disease and the failure of automated systems to identify *Y. pestis* reliably.

Both plague patients presented with fever; 1 had inguinal lymphadenopathy and the other had inguinal pain. Throughout enzootic areas, recognition of symptoms indicative of plague is critical for appropriate medical and public health responses and for guiding the clinical laboratory about diagnostic testing and specimen handling. Although a gram-negative organism with bipolar staining was visible in a blood culture from the Oregon patient, *Y. pestis* was not suspected. However, bipolar staining on Gram or Wright stains is not pathognomonic for *Y. pestis;* other gram-negative organisms (eg, *Enterobacteriaceae* and *Pasteurella* species) might also exhibit this characteristic [7].

Automated bacterial identification systems increasingly are used in clinical microbiology laboratories to provide rapid identification, thus reducing turnaround times and improving efficiency and cost-effectiveness [8]. These systems automatically perform 3 major functions for identification: monitoring biochemical reactions during growth of an isolate (eg, lactose fermentation, catalase positivity, and oxidase positivity); comparison of an isolate's characteristics with data for multiple organisms in the system's database; and completion of computerized calculations to determine the probability of identification, or confidence value, based on the patterns of biochemical results. These systems allow accurate and rapid identification of commonly isolated bacterial organisms; however, they are less likely to correctly identify slow-growing, fastidious, rare, or biochemically inert organisms, including select agents such as *Francisella tularensis*, *Burkholderia pseudomallei*, *Brucella* species, and *Y. pestis* [6, 9]. Indications of potential misidentification by automated systems include

a low probability or confidence value, an identification of a pathogen inconsistent with the clinical or microbiology picture, or both.

Results from automated systems should be analyzed critically, taking into consideration the reliability of these systems for accurate identification of slow-growing and/or rare organisms. In clinical microbiology laboratories, gram-negative isolates that exhibit bipolar staining and are pinpoint (slow-growing) colonies at 24 hours, nonlactose fermenters, and catalase-positive but urease- and oxidase-negative should trigger immediate consideration of *Y. pestis*, particularly in enzootic areas. If suspicion arises for *Y. pestis*, the state public health department should be contacted, and the isolate should be sent to the state public health laboratory for further testing.

CONCLUSIONS

Although plague is rare in the United States, it should be considered for patients who live in or have recently traveled to enzootic regions and present with fever and painful, swollen lymph nodes, or pneumonia. Clinicians and microbiologists should be aware of the potential for *Y. pestis* misidentification by automated systems. Identification of unusual organisms (eg, *P. luteola*, *Y. pseudotuberculosis*, or *A. lwoffii*) from the blood of patients with plague-compatible symptoms using automated systems should trigger further clinical and laboratory evaluation. If plague is suspected, appropriate treatment should be started immediately and isolates sent to public health laboratories for confirmation.

Notes

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